

What is Claimed Is:

1. A method to identify a therapeutic or prophylactic agent that modulates the response of a lymphocyte population to an antigen, comprising the steps of:
 - 5 preparing a first gene expression profile of a quiescent lymphocyte population;
 - preparing a second gene expression profile of a lymphocyte population exposed to the antigen;
 - treating the exposed lymphocyte population with a candidate compound;
 - 10 preparing a third gene expression profile of the treated lymphocyte population;
 - comparing the first, second and third gene expression profiles; and
 - identifying as a therapeutic or prophylactic agent a compound that modulates the response of a lymphocyte population to the antigen.
2. The method of claim 1, wherein the lymphocyte is a T lymphocyte.
- 15 3. The method of claim 1, wherein the lymphocyte is a B lymphocyte.
4. The method of claim 2, wherein the T lymphocyte population is selected from the group consisting of a population of T_{H1} , T_{DTH} , T_{CTL} , T_{H2} , T_S , memory T lymphocytes, effector T lymphocytes, pre-T lymphocytes, cortical T lymphocytes, medullary T lymphocytes, peripheral T lymphocytes, activated T lymphocytes,
- 20 quiescent T lymphocytes, and neoplastic T lymphocytes.

The method of claim 3, wherein the pathogen is selected from the group consisting of bacteria, viruses, parasites, mycoplasma, protozoans, and fungi.

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5. The method of claim 2, wherein the antigen is selected from the group consisting of a pathogen, an antigen derived from a pathogen, an allergen, a superantigen or self-antigen.

6. The method of claim 5, wherein the pathogen is selected from the group
5 consisting of bacteria, viruses, parasites, mycoplasma, protozoans, and fungi.

7. The method of claim 6, wherein the virus is selected from the group consisting of EBV, HIV-1, HTLV-I, HTLV-II, rabies virus, mouse mammary tumor virus, cytomegalovirus, poliovirus, Group C adenoviruses, herpes simplex virus, cytomegalovirus, rubella, measles, mumps, respiratory syncytial virus, vesicular
10 stomatitis virus, influenza A, parainfluenza, and lymphocytic choriomeningitis virus.

8. The method of claim 2, wherein the T lymphocyte population is exposed to the antigen associated with major histocompatibility molecules.

9. The method of claim 8, wherein the major histocompatibility molecules are exposed on the surface of antigen presenting cells.

15 10. The method of claim 8, wherein the major histocompatibility molecules are selected from the group consisting of Class I MHC and Class II MHC.

11. The method of claim 9, wherein the antigen presenting cells are selected from the group consisting of B lymphocytes, macrophages and dendritic cells.

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12. A method to identify a therapeutic or prophylactic agent that modulates a T lymphocyte population found in a subject having a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD comprising the steps of:

- 5 preparing a first gene expression profile of a T lymphocyte population in a subject having the sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD;
- treating the T lymphocyte population with a candidate compound;
- preparing a second gene expression profile of the treated T lymphocyte population;
- 10 comparing the first and second gene expression profiles with a gene expression profile of a normal T lymphocyte population; and
- identifying as a therapeutic or prophylactic agent a compound that modulates a T lymphocyte population found in a subject having a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD.

13. The method of claim 12, wherein the T lymphocyte population is selected from the group consisting of a population of T_{HI} , T_{DTH} , T_{CTL} , T_{H2} , T_S , memory T lymphocytes, effector T lymphocytes, pre-T lymphocytes, cortical T lymphocytes, medullary T lymphocytes, and peripheral T lymphocytes.
- 20 14. The method of claim 12, wherein the sterile inflammatory disease is selected from the group consisting of psoriasis, rheumatoid arthritis, glomerulonephritis, asthma, allergic rhinitis, cardiac and renal reperfusion injury, thrombosis, adult respiratory distress syndrome, inflammatory bowel disease, Crohn's

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disease, ulcerative colitis, periodontal disease, lymphocytopenias, autoimmune lymphoproliferative syndrome, synovitis, sarcoidosis, DiGeorge's syndrome, Nezelof syndrome, severe combined immunodeficiency syndromes, Wiskott-Aldrich syndrome, Ataxia-telangiectasia, Cartilage-hair hypoplasia, immunodeficiency with

5 thymoma, and leukocyte adhesion deficiency 1.

15. The method of claim 12, wherein the cancer is selected from the group consisting of: precursor T-lymphoblastic lymphoma/leukemia, T lymphocyte chronic lymphocytic leukemia/prolymphocytic leukemia, T lymphocyte type large granular lymphocyte leukemia, Mycosis fungoides/Sezary syndrome, unspecified peripheral T 10 lymphocyte lymphomas, angioimmunoblastic T lymphocyte lymphoma, nasal type T/NK cell (angiocentric) lymphoma, intestinal T lymphocyte lymphoma with or without associated enteropathy, hepatosplenic $\gamma\delta$ T lymphocyte lymphoma, subcutaneous panniculitic T lymphocyte lymphoma, adult T lymphocyte lymphoma/leukemia, anaplastic large cell lymphoma, T lymphocyte hairy cell 15 leukemia, and T lymphocyte chronic lymphocytic leukemia.

16. The method of claim 12, wherein the immunodeficiency disease or autoimmune disorder is selected from the group consisting of: rheumatoid arthritis, spondyloarthropathies, systemic lupus erythematosus, HIV-1, polymyositis, inclusion body myositis, SCIDs, Wiskott-Aldrich syndrome, Swiss-type agammaglobulinemia, 20 thymic alymphoplasia, Ataxia Telangiectasia, bare lymphocyte syndrome, immune deficiency with thymoma, transient hypogammaglobulinemia of infancy, DiGeorge's syndrome, Nezelof's syndrome, autosomal recessive lymphopenia with normal or

abnormal immunoglobulins, Omenn's syndrome, and idiopathic CD4+ lymphocytopenia.

17. A article of manufacture comprising a grouping of nucleic acids affixed to a solid support, said nucleic acids corresponding to genes whose expression levels are modulated in a T lymphocyte population that has been exposed to an antigen.

18. An article of manufacture comprising a grouping of nucleic acids affixed to a solid support, said nucleic acids corresponding to genes whose expression levels are modulated in a T lymphocyte population found in a subject having a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD.

19. A method of diagnosing exposure of a subject to an antigen comprising the steps of:

preparing a first gene expression profile of a T lymphocyte population from the subject;

comparing the first gene expression profile to a second gene expression profile of a T lymphocyte population exposed to an antigen and to a third gene expression profile of a normal T lymphocyte preparation; and

determining if the subject was exposed to an antigen.

20. The method of claim 19, wherein the antigen is a pathogen, antigen derived from a pathogen, allergen, superantigen or self-antigen.

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21. A method of diagnosing a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD in a subject, comprising the steps of:

- preparing a first gene expression profile of a T lymphocyte population from the subject;
- comparing the first gene expression profile to at least one second gene expression profile from a T lymphocyte population from a subject having a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD and to a third gene expression profile of a normal T lymphocyte population;
- and
- determining if the subject has a sterile inflammatory disease, autoimmune disorder, immunodeficiency disease, cancer, or GVHD.

22. A method to identify a therapeutic or prophylactic agent that modulates a T lymphocyte population that arises from a genetic defect, comprising the steps of:

- 15 preparing a first gene expression profile of a T lymphocyte population that arises from the genetic defect;
- treating the first T lymphocyte population with the agent;
- preparing a second gene expression profile of the treated T lymphocyte population;
- 20 comparing the first and second gene expression profiles with a gene expression profile of a normal T lymphocyte population; and

identifying agents that modulate a T lymphocyte population that arises from a genetic defect.

23. The method of claim 22, wherein the T lymphocyte population is selected from the group consisting of a population of T_{H1} cells, T_{H2} cells, T_{DTH} cells,
5 T_{CTL} cells, T_S cells, memory T lymphocytes, effector T lymphocytes, pre-T lymphocytes, cortical T lymphocytes, medullary T lymphocytes, peripheral T lymphocytes, neoplastic cells, LAK cells, and TIL cells.

24. The method of claim 22, wherein the genetic disease is selected from the group consisting of: irritated valve disease, Crohn's disease, asthma,
10 lymphocytopenia, autoimmune lymphoproliferative syndrome, rheumatoid arthritis, DiGeorge syndrome, Nezelof syndrome, SCIDs, Wiskott-Aldrich syndrome, Ataxia-telangiectasia, Cartilage-hair hypoplasia, immunodeficiency with thymoma, leukocyte adhesion deficiency 1, graft vs. host disease, non-Hodgkin's lymphoma, Hodgkin's disease, cutaneous T lymphocyte lymphoma, adult T-cell leukemia/lymphoma,
15 anaplastic large cell lymphoma, chronic lymphocytic leukemia, prolymphocytic leukemia, small cell cerebriform (mycosis fungoides, Sezary syndrome), lymphoepithelioid (Lennert's lymphoma), angioimmunoblastic (AILD, LgX), T-zone lymphoma, pleomorphic — small cell (HTLV-I ±).

25. A article of manufacture comprising a grouping of nucleic acids
20 affixed to a solid support, said nucleic acids corresponding to genes whose expression levels are modulated in a T lymphocyte population that contains a genetic defect.

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26. A method to identify an agent that induces the differentiation of quiescent pre-T lymphocytes, cortical T lymphocytes or medullary T lymphocytes into a differentiated T lymphocyte subpopulation, comprising the steps of:

5 preparing a first gene expression profile of a quiescent pre-T lymphocyte population, cortical T lymphocyte population or medullary T lymphocyte population;

10 preparing a second gene expression profile of a quiescent pre-T lymphocyte population, cortical T lymphocyte population or medullary T lymphocyte population exposed to a candidate compound;

15 preparing a third gene expression profile of a differentiated T lymphocyte population;

comparing the first, second and third gene expression profiles; and identifying as an agents a compound that induces differentiation.

27. The method of claim 26, wherein the differentiated T lymphocyte population is selected from the group consisting of a population of T_{H1} cells, T_{H2} cells, $T_{DT\bar{H}}$ cells, T_{CTL} cells, T_S cells, memory T lymphocytes and effector T lymphocytes.

28. An isolated nucleic acid molecule comprising a DNA molecule selected from the group consisting of: (1) the DNA molecules of SEQ ID NOS. 16, 20 22, 24, 25, 31, 33, and 34; and (2) a nucleic acid that specifically hybridizes to any one of the DNA molecules of SEQ ID NOS. 16, 22, 24, 25, 31, 33, and 34.

29. The isolated nucleic acid fragment of claim 26 which consists of any one of the DNA molecules of SEQ ID NOS. 16, 22, 24, 25, 31, 33, and 34.

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30. The isolated nucleic acid of claim 26, wherein the specifically hybridizing nucleic acid is of the form R-X-R'

wherein X is any one of the DNA molecules of SEQ ID NOS.16, 22, 24, 25, 31, 33, and 34;

5 wherein R and R' are sequences contiguous with X; and
 wherein R and R' may or may not be contiguous.

31. A vector comprising the isolated nucleic acid molecule of any one of claims 28 to 30.

32. A transformed host cell comprising the vector of claim 31.
10 33. The isolated nucleic acid molecule of claim 28, comprising the DNA molecule of SEQ ID NO. 34 or a nucleic acid that specifically hybridizes to that DNA molecule.

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